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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/260,468	03/02/99	ROBL J	000270 - 057

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EXAMINER	
MARTIN, J	
ART UNIT	**PAPER NUMBER**
1632	13

DATE MAILED: 06/21/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/260,468	ROBL ET AL.	
	Examiner	Art Unit	
	Jill Martin	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-19,21-30 and 32-57* is/are pending in the application.

4a) Of the above claim(s) *26-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-19,21-30 and 32-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☒ The proposed drawing correction filed on *03-02-99* is: a)☐ approved b)☒ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☐ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

Applicants' Amendment filed April 12, 2001 (Paper No. 11) has been entered. Claims 3, 20, and 31 have been canceled, claims 1, 15, 16, 18, 19, 21, 22, 23, 32, 33, and 35 have been amended, and claims 51-57 have been added. Claims 1, 2, 4-19, 21-30, and 32-57 are pending, however, Claims 26-30 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. Election was made **without** traverse in Paper No. 8. Note that a complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Double Patenting

The prior double patenting rejection of 1, 15, 16, 18, 19, 21, 22, 23, 32, 33, and 35, and new claims 51-57 is maintained for the reasons of record advanced on pages 2-3 of the prior Office action mailed 10/13/00 (Paper No. 10).

Applicants request that the rejection be held in abeyance until allowance is negotiated. See Amendment page 5.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The prior rejection of claims 18, 19, and 21-23, and new claims 51 and 57 is maintained for being directed to non-statutory subject matter for the reasons advanced on page 3 of the prior Office action.

Applicants indicate that the claims have been amended to now refer to an embryonic stem-like cell to further clarify that the phrase is not intended to encompass an actual embryo.

In response, it is noted that the claims still do not differentiate the embryonic stem-like cell from an embryonic cell that is a one, two, or three cell embryo, for example.

Accordingly, the prior rejection of the claims under 101 for being directed to non-statutory subject matter stands.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior enablement rejection of claims 1, 15, 16, 18, 19, 21, 22, 23, 32, 33, and 35, and new claims 51-57 is maintained for the reasons advanced on pages 4-11 of the prior Office action mailed 10/13/00 (Paper No. 10).

Applicants initially point the Examiner to the amendments to the claims, and remark that the limitation to the preamble of claim 1 emphasizes that the cells comprise a nucleus from an adult differentiated cell and mitochondria from an oocyte of a species other than said adult

differentiated cell thereby distinguishing the cells made by the method from embryonic stem cells as known in the art. See page 7 of the Amendment.

In response, the claim amendments and additions are acknowledged, but do not reduce any of the issues on the record under enablement, particularly since the claim amendments do little towards the use of the cells for cloning humans with non-human mitochondria. Rather, such amendments further contribute to the issues set forth under enablement. Namely, the specification fails to provide direction or guidance for the transplantation of a stem cell or cells differentiated therefrom containing exogenous mitochondria.

More particularly, the cited art (Takeda et al., Evans et al., & Lanza et al., pages 7-8 of the Amendment) supports the claim amendments with regard to obtaining embryos, and animals having mitochondria derived from the oocyte. As such, it is reiterated that the claim amendments do little towards removing the issue of cloning humans with non-human mitochondria, particularly since there is no guidance or direction for use of the stem cells or cells differentiated therefrom having exogenous mitochondria in transplantation therapy.

Applicants discuss the Lanza et al. reference with regard to the cloned gaur, and speculate that the results can reasonably be extended to the production of human differentiated tissues, particularly when supplemented with the specification which teaches an NT unit using a human somatic cell nucleus and bovine oocyte. Applicants go on to assert that such tissues would be ideally suited for transplantation and cell therapies given that the tissues may be designed using a

cell or nucleus from the patient in need of such transplantation therapy. See page 8 of the Amendment.

In response, it is noted that Applicants' speculation and assertion fail to be supported by any sound reasoning. Rather, the cloned gaur data represent that phylogenetically similar species can contribute & differentiate into tissues of the whole animal (gaur). The claimed invention is not limited to phylogenetically similar species. The results disclosed within the specification fail to include any evidence with regard to differentiation of the cells cultured from the NT unit. Rather, the specification lacks any showing of any relevant information which could positively identify the cells. See page 5 of the prior Office action. See also pages 9-10 of the prior Office action, wherein Marshall supports that the skilled artisan had stated that the cells in question had not met the criteria for embryonic stem cells.

Applicants go on to indicate that it would be possible to perform cross-species nuclear transfer using recipient oocyte or other suitable cell from a species more evolutionarily related to human. Here, Applicants refer to evidence primordial germ cell culture of cynomologous monkeys. See pages 9-10 of the Amendment.

In response, while this indication is true, none of the claims are directed to this limitation. Rather, certain of the claims are specifically limited to human/bovine cross-species nuclear transfer and resulting cells, and many of the claims encompass even more evolutionarily distinct species for that matter. See for example claim 52 which recites that the adult differentiated cell and enucleated oocyte are phylogenetically dissimilar. As such, the submitted evidence with

regard to the culture of primate primordial germ cells and the differentiation thereof really are not relevant to the claims which require resulting cells having a nucleus from one species and mitochondria from another.

Applicants argue that other Patents have not been held to the same standard of being useful for the production of cloned humans, citing US Patent 6,200,806.

In response, with regard to claim breadth, the standard under 112, first paragraph entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the enabled scope of the claims, the teachings of the specification are taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification. Therefore, proper examination of the claims under 112, first paragraph, should encompass the use of the ES-like cells for germline manipulation as the specification discusses this at pages 2-6. See page 9 of the prior Office action. With regard to the '806 Patent, each Patent is examined on its own merits. However, it is noted that the claims are directed to purified preparations of pluripotent human embryonic stem cells and methods of isolating the same. Pluripotency is not an indication of totipotency, *i.e.*, contribution to the germ line. The instant claims are directed to cross-species nuclear transfer methods and cells having distinct nuclear and mitochondrial DNA. New claims 53-57 still encompass this embodiment, despite that they lack the terminology "ES-like", and thus, still must be read in light of the specification which discusses use of the cells for germline manipulation.

Applicants argue that the methods and cells find uses in the art other than their use for differentiation assays, citing for use in the study of genes involved in early development, or for use as a model for deciphering the role of mitochondrial genes in mammalian development and cellular function, for example. See paragraph bridging pages 9-10 of the Amendment.

In response, this is the Examiner's point exactly, that is, that the claims find use in delineating their use. A need for delineation of a final product claimed invention, indicates that the specification fails to fulfill the requirements for how to make and how to use the claimed invention, particularly in an unpredictable and extremely undeveloped art, and more particularly since the disclosure of how to use such embryonic-like cells falls within the field of another unpredictable art, germline manipulation. See the specification at pages 2-6. Furthermore, with regard to the discussion of "how to use" such cells for "model systems" for research, it is held that even model systems are not found to be enabled by a specification which requires a need for delineation of the model system itself.

Applicants conclude that the gene-modified differentiated cells are enabled as gene modification has been known in the art for year. See pages 10-11 of the Amendment.

In response, Applicants are referred to page 10 of the prior Office action. While gene modification of many cell types has been known in the art, the specifically claimed cells (prior to gene modification) have not been delineated. In fact, the specification fails to teach gene modification of any cell produced by their methods, and fails to teach a gene-modified differentiated cell as a starting point for nuclear transfer. Furthermore, the claims are read in light

of the specification, and such gene-modified cells are included in the interpretation set forth above based upon the discussion of the specification drawn to germline manipulation.

Accordingly, the enablement rejection of record is maintained for the reasons of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The prior rejection of claims 1, 15, 16, 18, 19, 21, 22, 23, 32, 33, and 35, and new claim 51, as failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

In these claims, it is maintained that the limitation "embryonic or stem-like cells" is vague and indefinite for the reasons advanced on page 11-12 of the prior Office action. It appears that Applicants refer to the claims as being directed to "embryonic stem-like cells" without the "or". This is not the case for the pending claims. To this end, while the limitation directed to the mitochondria clarify the structural characteristics of the cells, it fails to remove the ambiguity of the embryonic or stem-like properties of the cells Applicant is referring to as "embryonic or stem-like". To this end, it is unclear how the structural characteristics now recited in the claims relate to the terminology "embryonic or stem-like". Furthermore, removal of the "or" fails to remove the interpretation of the cells reading on embryos since, for instance, embryos can be 1 celled.

Claim Rejections - 35 USC § 102 & 103

The prior 102 & 103 rejections of record have been withdrawn in view of Applicants amendments to the claims requiring that the structural characteristics of the cells include species distinct nuclear and mitochondrial DNA.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

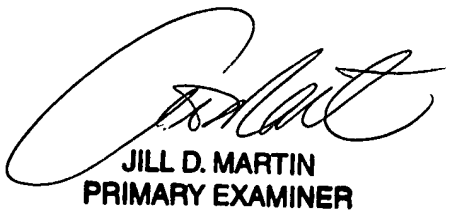
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jill Martin whose telephone number is (703)305-2147.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached at (703)305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Kay Pinkney, whose telephone number is (703)305-3553.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.



Jill D. Martin
Primary Examiner
Art Unit 1632